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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,999	03/12/2007	Julia Y. Ljubimova	67789-118US0	9455

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EXAMINER	
EPPS -SMITH, JANET L	

ART UNIT	PAPER NUMBER
1633	

NOTIFICATION DATE	DELIVERY MODE
03/05/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/580,999	LJUBIMOVA ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Smith	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13, 18-23* is/are pending in the application.

4a) Of the above claim(s) ___ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 18-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/01/2010 has been entered.

2. Claims 1-13 and 18-23 are pending and are under examination.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Priority

4. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) to provisional application 60/527,300 is acknowledged.

Claim Rejections - 35 USC § 103 - Maintained

5. Claims 1-13 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over LaFleur, et al. (10/29/2002, U.S. Patent 6,472,512) and Cammas, et al. (1999, Internat. J. Biol. Macromol., v.25:273-82, item 55 on 11/08/2007 IDS) (Cammas). This rejection is maintained for the reasons of record.

6. Applicant's arguments filed 02/01/2010 have been fully considered but they are not persuasive. Applicants argue that Cammas et al. does not teach covalent

attachment to the claimed active modules and that Examiner fails to understand some of the differences between the prior art and the present invention as claimed.

7. Applicants further argued the following: "[I]n this instance, Applicants submit that the combination of Cammas, et al, and LaFleur et al. would produce a seemingly inoperative device. Cammas et al. describes synthesis of various forms of polymalic acid conjugated to conjugates by anionic ring-opening polymerization of maloactonic acid esters appropriately derivatized at the alpha-carboxylic group in the monomer before polymerization. Attachment of proteins and nucleic acids via ring open polymerization of corresponding malolactonic derivatives, such as that described by Cammas et al., is not chemically possible. The product would be inactive in targeted drug delivery…"

8. Contrary to Applicant's assertions, as per MPEP § 2145[R-6], "[a]rguments of counsel cannot take the place of factually supported objective evidence." "[T]he arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965).

9. Applicant's assertion that the attachment of proteins and nucleic acid via ring open polymerization of malolactonic derivatives, such as that described by Cammas et al. "is not chemically possible," and further that the "product would be inactive in targeted drug delivery," is a statement that must be supported by an appropriate affidavit or declaration.

10. As per MPEP § 716.01(c) [R-2], "[O]bjective evidence which must be factually supported by an appropriate affidavit or declaration to be of probative value includes

evidence of unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant. See, for example, In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984) ("It is well settled that unexpected results must be established by factual evidence." "[A]ppellants have not presented any experimental data showing that prior heat-shrinkable articles split. Due to the absence of tests comparing appellant's heat shrinkable articles with those of the closest prior art, we conclude that appellant's assertions of unexpected results constitute mere argument.").

11. Applicants further argued that the "present application describes how to covalently attach a plurality of durable (e.g. PEG, amino acid, spacers) and non durable (e.g. proteins and nucleic acids) molecules in a hierarchic mode to polymalic acid, starting with highly purified naturally occurring beta-poly(L-malic acid) produced by Physarum polycephalum."

12. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., that the claimed drug delivery vehicle are produced starting with highly purified naturally occurring beta-poly(L-malic acid) produced by Physarum polycephalum) is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

13. Moreover, at page 7 of Applicant's reply filed 02/01/2010, Applicants argue that the present invention differs from the prior art to the extent that the method of synthesis of the claimed delivery vehicles is distinct from the methods set forth in the prior art. Again, as stated above, limitations from the specification are not read into the claims. The features upon which Applicants rely, namely the method of synthesis set forth in the specification as filed, is not set forth in the instant claims.

14. Claims 1-13 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over LaFleur, et al. (10/29/2002, U.S. Patent 6,472,512) and Cammas, et al. (1999, Internat. J. Biol. Macromol., v.25:273-82, item 55 on 11/08/2007 IDS) (Cammas) as applied to claims 1-13 and 20 above, and further in view of Saito, et al. (2003, Adv. Drug Del. Rev., v.55:199-215, item 63 on 11/08/2007 IDS) (Saito). This rejection is maintained for the reasons of record.

Response to arguments

15. Applicant's arguments regarding this rejection have been addressed in the preceding rejection.

16. Claims 1-13, 20, and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over LaFleur, et al. (10/29/2002, U.S. Patent 6,472,512) and Cammas, et al. (1999, Internat. J. Biol. Macromol., v.25:273-82, item 55 on 11/08/2007 IDS) (Cammas) as applied to claims 1-13 and 20 above, further in view of Summerton, et al. (1997, Nuc. Acid Drug Dev., v.7:187-95, item 38 on 11/08/2007 IDS) (Summerton). This rejection is maintained for the reasons of record.

Response to arguments

17. Applicant's arguments regarding this rejection have been addressed in the preceding rejection.

18. Claims 1-13, and 20-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over LaFleur, et al. (10/29/2002, U.S. Patent 6,472,512) and Cammas, et al. (1999, Internat. J. Biol. Macromol., v.25:273-82, item 55 on 11/08/2007 IDS) (Cammas) as applied to claims 1-13 and 20 above, further in view of Khazenzon, et al. (2003, Mol. Cancer Ther., v.2:985-94, item 47 on 11/08/2007 IDS) (Khazenzon). This rejection is maintained for the reasons of record.

Response to arguments

Applicant's arguments regarding this rejection have been addressed in the preceding rejection.

Claim Rejections - 35 USC § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

20. Claims 1, and 18-20 are rejected under 35 U.S.C. 102(a) as being anticipated by Bulmus et al.

(Journal of Controlled Release 93 (November 18, 2003) 105–120.

21. Bulmus et al. teach a drug delivery molecule comprising polymerized carboxylic acid having a plurality of free carboxylic acid groups, at least one polynucleotide and at least one targeting molecule. At page 111, the following is disclosed:

In this study, a glutathione-sensitive, functionalized, ''smart'' polymer with pH-dependent membrane-disruptive activity was designed as a delivery vehicle for the enhanced cytoplasmic delivery of biomolecular drugs such as asODNs, proteins and peptides. This polymer is composed of a backbone of methacrylic acid (MAAc), butyl acrylate (BA) and pyridyl disulfide acrylate (PDSA) units (Fig. 1). Acidic (MAAc) and hydrophobic (BA) monomers were the main components of the polymer and chosen to constitute a pH-responsive, membrane-disruptive backbone. PDSA, a novel functional monomer, was incorporated into the pH-sensitive backbone to allow for the easy conjugation of therapeutic biomolecules through the cleavable disulfide bonds under mild reaction conditions. Disulfide bonds have been shown to be stable in the blood stream [22,23]. The release of the drug conjugated to the polymer is expected to occur by reduction of the disulfide bond upon exposure of the conjugate to intracellular thiols such as glutathione or redox enzymes, which are present at high concentrations in the cytoplasm of the cells [24]. A targeting agent that directs receptor-mediated endocytosis (RME) can be easily incorporated into the polymer through the functional PDSA component using a variety of chemistries, including disulfide or thioether bond formation.

Moreover, at page 117, the following is disclosed:

To investigate cell uptake of poly(MAAc-co-BAco-PDSA), in a preliminary experiment, THP-1 macrophage-like cells were contacted with ^{14}C-labeled-poly(MAAc-co-BA-co-PDSA) at two different concentrations in 10% serum containing media for 4 h. The terpolymer used in this experiment has MAAc/BA mole ratio of 77:23, PDSA mol% of 3 and MWof 100,000. Since the THP-1 macrophage-like cells are phagocytic, no cell receptor targeting ligand was utilized. The radioactivity levels taken up by the cells were normalized to the total protein amount. The uptake of the terpolymer into the THP-1 cells was observed as a function of polymer concentration (Table 3). This result provided preliminary support for the usability of this novel polymer in the delivery of biotherapeutics to macrophages that play an important role in many inflammatory diseases. We are currently investigating the uptake of terpolymer–asODN disulfide bond conjugates, with and without a receptor targeting ligand, i.e. mannose, in the same macrophage like cell line.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Smith whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Smith/
Primary Examiner, Art Unit 1633